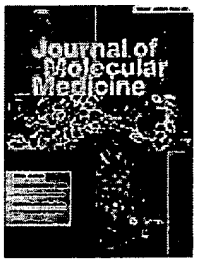
Exhibit I



Journal Article




# The clinical significance of prostaglandins and thromboxane as mediators of septic shock

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Summary An evaluation was made of 106 surgical patients with Gram-negative septic shock, both for clinical criteria as well as the biochemical mediators endotoxin, prostaglandin $F_{2\alpha}$, prostaglandin $I_2$ (prostacyclin), and thromboxane. These data were correlated to various defined shock phases, functional data of vital organs, and clinical outcome. Patients underwent

invasive organ function monitoring and the usual laboratory tests of intensive care. Prostaglandins and thromboxane were measured radioimmunologically, endotoxin by the limulus amebocyte lysate test. Endotoxin proved to be a more accurate predictor of severe sepsis than did positive blood cultures. Endotoxin as well as prostaglandins and thromboxane are predominantly released in early shock phases, appearing in plasma concentrations, which correlate with the severity of organ failure. Sepsis-induced respiratory failure coincides with a deterioration of pulmonary prostaglandin inactivation, which contributes to the release mechanism. High systemic prostacyclin activity benefits the patients' organ functions and clinical outcomes, while a predominance of thromboxane seems to effect the opposite. Transpulmonary-thromboxane gradients correlate significantly with pulmonary hypertension in the early phases of septic shock.

Key words Septic shock - Endotoxin - Eicosanoids - Prostaglandins - Thromboxane

Abbreviations $AaDO_2$ Alveolar-arterial $O_2$ gradient - AAS Arachidonic acid system - ARDS Acute respiratory distress syndrome - CI Cardiac index - CrCl Creatinine clearance - DIC Disseminated intravascular coagulation - EU Endotoxin unit - EU/ml Endotoxin unit per milliliter - HYPER Hyperdynamic shock - HYPO Hypodynamic septic shock - $KH_2PGF_{2\alpha}$ 13,14-Dihydro-15-Keto-$PGF_{2\alpha}$ - 6-K-

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$PGF_{1\alpha}$ 6-Keto-$PGF_{1\alpha}$ - LPS Lipopolysaccharide - MABP Mean arterial blood pressure - Norm Normal values - PG Prostaglandin - pg/ml Picogram per milliliter - $PGI_2$ Prostacyclin - PVR Pulmonary vascular resistance - SVR Systemic vascular resistance - TX Thromboxane

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References secured to subscribers.